Guidelines for Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults and Adolescents

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Table 4. Indications for Discontinuing and Restarting Opportunistic Infection Secondary Prophylaxis or Chronic Maintenance in HIV-Infected Adults and Adolescents (page 1 of 3) (Last updated November 10, 2016; last reviewed November 10, 2016)

Opportunistic Infection	Indication for Discontinuing Primary Prophylaxis	Indication for Restarting Primary Prophylaxis	Indication for Discontinuing Secondary Prophylaxis/ Chronic Maintenance Therapy	Indication for Restarting Secondary Prophylaxis/Chronic Maintenance
***Pneumocystis* Pneumonia**	CD4 count increased from <200 to >200 cells/μL for >3 months in response to ART **(AI)**	CD4 count <200 cells/mm^3 **(AIII)**	CD4 count increased from <200 cells/μL to >200 cells/μL for >3 months in response to ART **(BII)** If PCP was diagnosed when CD4 count was >200 cells/μL, continue prophylaxis for life regardless of CD4 count rise in response to ART **(BIII)**.	• CD4 count <200 cells/μL **(AIII)**, *or* • If PCP recurred at CD4 count >200 cells/μL, prophylaxis should be continued for life **(CIII)**.
***Toxoplasma gondii* Encephalitis**	CD4 count increased to >200 cells/μL for >3 months in response to ART **(AI)**	CD4 count <100 to 200 cells/μL **(AIII)**	Successfully completed initial therapy, remain free of signs and symptoms of TE, and CD4 count >200 cells/μL for >6 months in response to ART **(BI)**.	CD4 count <200 cells/μL **(AIII)**
Microsporidiosis	Not applicable	Not applicable	No signs and symptoms of non-ocular **(BIII)** or ocular **(CIII)** microsporidiosis and CD4 count >200 cells/μL for >6 months in response to ART.	No recommendation
Disseminated *Mycobacterium avium* Complex Disease	CD4 count >100 cells/μL for ≥3 months in response to ART **(AI)**	CD4 count <50 cells/μL **(AIII)**	If the following criteria are fulfilled **(AI)**: • Completed ≥12 months of therapy, *and* • No signs and symptoms of MAC disease, *and* • Have sustained (>6 months) CD4 count >100 cells/μL in response to ART.	CD4 count <100 cells/μL **(AIII)**
Salmonellosis	Not applicable	Not applicable	Resolution of *Salmonella* infection and after response to ART with sustained viral suppression and CD4 counts >200 cells/μL **(CII)**	No recommendation
Bartonellosis	Not applicable	Not applicable	• Received at least 3–4 months of treatment, *and* • CD4 count >200 cells/μL for ≥6 months **(CIII)** • Some specialists would only discontinue therapy if *Bartonella* titers have also decreased by four-fold **(CIII)**.	No recommendation
Mucosal Candidiasis	Not applicable	Not applicable	If used, reasonable to discontinue when CD4 count >200 cells/μL **(AIII)**.	No recommendation

Table 4. Indications for Discontinuing and Restarting Opportunistic Infection Secondary Prophylaxis or Chronic Maintenance in HIV-Infected Adults and Adolescents (page 2 of 3)

Opportunistic Infection	Indication for Discontinuing Primary Prophylaxis	Indication for Restarting Primary Prophylaxis	Indication for Discontinuing Secondary Prophylaxis/ Chronic Maintenance Therapy	Indication for Restarting Secondary Prophylaxis/Chronic Maintenance
Cryptococcal Meningitis	Not applicable	Not applicable	If the following criteria are fulfilled **(BII)**: • Completed initial (induction and consolidation) therapy, *and* • Received at least 1 year of maintenance therapy, *and* • Remain asymptomatic of cryptococcal infection, *and* • CD4 count ≥100 cells/μL for >3 months, and with suppressed plasma HIV RNA in response to ART	CD4 count <100 cells/μL **(AIII)**
***Histoplasma capsulatum* Infection**	CD4 count >150 cells/μL for 6 months while on ART **(BIII)**	For patients at high risk of acquiring histoplasmosis, restart at CD4 count <150 cells/μL **(CIII)**	If the following criteria **(AI)** are fulfilled: • Received itraconazole for >1 year, *and* • Negative fungal blood cultures, *and* • CD4 count ≥150 cells/μL for ≥6 months in response to ART, *and* • Serum *Histoplasma* antigen <2 ng/mL	CD4 count <150 cells/mm^3 **(BIII)**
Coccidioido-mycosis	CD4 count ≥250 cells/μL and with viral suppression while on ART **(CIII)**	Restart at CD4 count <250 cells/μL **(BIII)**	Only for patients with focal coccidioidal pneumonia **(AII)**: • Clinically responded to ≥ 6 months antifungal therapy, with CD4 count ≥250 cells/mm^3, and with viral suppression while on ART. • Should continue monitoring for recurrence with serial chest radiographs and coccidioidal serology every 6-12 months. For patients with diffuse pulmonary **(BIII)**, disseminated non-meningeal **(BIII)**: • Therapy is at least 12 months and usually much longer; discontinuation is dependent on clinical and serological response and should be made in consultation with experts For meningeal diseases **(AII)**: Suppressive therapy should be continued indefinitely, even with increase in CD4 count on ART.	No recommendation

Table 4. Indications for Discontinuing and Restarting Opportunistic Infection Secondary Prophylaxis or Chronic Maintenance in HIV-Infected Adults and Adolescents (page 3 of 3)

Opportunistic Infection	Indication for Discontinuing Primary Prophylaxis	Indication for Restarting Primary Prophylaxis	Indication for Discontinuing Secondary Prophylaxis/ Chronic Maintenance Therapy	Indication for Restarting Secondary Prophylaxis/Chronic Maintenance
Cytomegalovirus Retinitis	Not applicable	Not applicable	• CMV treatment for at least 3 to 6 months; and with CD4 count >100 cells/μL for >3 to 6 months in response to ART **(AII)**. • Therapy should be discontinued only after consultation with an ophthalmologist, taking into account anatomic location of lesions, vision in the contralateral eye, and feasibility of regular ophthalmologic monitoring. • Routine (i.e., every 3 months) ophthalmologic follow-up is recommended after stopping therapy for early detection of relapse or immune restoration uveitis, and then periodically after sustained immune reconstitution **(AIII)**.	CD4 count <100 cells/μL **(AIII)**
***Penicillium marneffei* Infection**	CD4 count >100 cells/μL for >6 months in response to ART **(BII)**	CD4 count <100 cells/μL **(BIII)**	CD4 count >100 cells/μL for ≥6 months in response to ART **(BII)**	• CD4 count <100 cells/μL (AIII), *or* • If penicilliosis recurs at CD4 count >100 cells/μL **(CIII)**
Visceral Leishmaniasis (and possibly cutaneous leishmaniasis in immunocompromised patients with multiple relapses)	Not applicable	Not applicable	There is no consensus regarding when to stop secondary prophylaxis. Some investigators suggest that therapy can be stopped if CD4 count increases to >200 to 350 cells/μL for 3–6 months in response to ART, but others suggest that therapy should be continued indefinitely.	No recommendation
***Isospora belli* Infection**	Not applicable	Not applicable	Sustained increase in CD4 count to >200 cells/μL for >6 months in response to ART and without evidence of *I. belli* infection **(BIII)**	No recommendation

Key to Acronyms: ART = antiretroviral therapy; CD4 = CD4 T lymphocyte cell; CMV = cytomegalovirus; MAC = *Mycobacterium avium* complex; PCP = *Pneumocystis* pneumonia; TE = *Toxoplasma* encephalitis

Evidence Rating:

Strength of Recommendation:

A: Strong recommendation for the statement
B: Moderate recommendation for the statement
C: Optional recommendation for the statement

Quality of Evidence for the Recommendation:

I: One or more randomized trials with clinical outcomes and/or validated laboratory endpoints
II: One or more well-designed, nonrandomized trials or observational cohort studies with long-term clinical outcomes
III: Expert opinion

In cases where there are no data for the prevention or treatment of an OI based on studies conducted in HIV-infected populations, but data derived from HIV-uninfected patients exist that can plausibly guide management decisions for patients with HIV/AIDS, the data will be rated as III but will be assigned recommendations of A, B, C depending on the strength of recommendation.